THE INFLUENCE OF WARMTH UPON THE IRRITABILITY OF FROG'S MUSCLE AND NERVE.

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HISTORICAL.

At the suggestion of Dr. Howell the following experiments were undertaken to demonstrate the effects of warmth upon the irritability of frog's muscle. The historical resumé is brief, for although a number of investigators have given hints, only two, Marey and Schmulewitsch, have given us important results concerning this phase of muscle activity.

Helmholtz,(1) whose classical researches have furnished the foundation for the modern investigation of muscle phenomena, seems not to have mentioned the influence of warmth, although he noticed that of cold, upon muscle contraction. E. J. Marey,(2) in 1868, with new and much improved methods, was enabled to record very elaborately his results.

The frog's gastrocnemius was placed in a metallic case surrounded by a second case, while in the annular space between the two warm water was made to flow. The effects of heating the muscle he divided into two periods. In the first, the period of "excitation of muscular action," the simple contraction is shorter and stronger as the temperature rises, provided, however, it does not exceed 30° to 35° C. In the second period, that of "alteration of the muscle by warmth, and loss of irritability," if the warmth be increased from the previous limit of 35° C., the height of the contraction decreases and the muscle does not regain its normal length, so that each contraction curve shows a marked contracture. If the muscle is warmed by submitting it immediately to a temperature of 45° to 50° C. this result of the second period may be obtained at once without the occurrence of the first period.

To these two periods a third should be added in the "*Nullpunkt*" of J. Schmulewitsch.(3) Schmulewitsch placed the frog's gastrocnemius in a vessel containing 0.65 per cent. NaCl solution,

over the rim of which the nerve was carried to the stimulating electrodes, so that it was not submitted to the same temperature as the muscle. The muscle was warmed by placing the vessel in which it was fastened in a larger vessel containing water of a constant temperature of from 46° to 47° C., by means of which it could be heated to any given temperature. At a certain temperature, varying with individual muscles from 37° to 41.5° C., the muscle loses its irritability—reaches the "*Null-punkt.*" The irritability could be restored by bringing the muscle to a lower temperature again. The cooling was done in one-half minute by means of fresh cool NaCl solution.

In Marey's results the gradual loss of irritability was associated with heat rigor. But the fact discovered by Schmulewitsch, and shown in this paper, that a complete loss of irritability can be obtained without any heat rigor, thus making the latter quite distinct, makes it necessary to add a fourth period, that of *heat rigor*, to the preceding.

According to Hermann,[4] heat rigor was first observed by Pickford.

Ch. Rouget[6] noticed that the extent of the heat rigor shortening is equal to that of the highest contraction, and he declared them to be of the same nature.

W. Preyer[7] found that after the muscle had gone into rigor its irritability could be regained if, in addition to restoring the circulation, the muscle was bathed in 10 per cent. NaCl or certain other solutions.

Apparatus.

The apparatus I used for warming the muscle consisted essentially of a double-walled brass cylinder, *b* of Plate IV, about 11.5 cms. long and 6 cms. wide. The distance between the outer and inner walls of the cylinder was 1 cm., and through this space warm or cool water was made to pass from a reservoir, *a*, in which the water was always kept some two or three degrees higher than that to which it was desired to have the cylinder heated. In this way the cylinder could be warmed slowly or quickly to any given point and, when desired, its temperature could be kept constant within half a degree for any length of time. The muscle to be warmed was placed within the space

enclosed by the inner cylinder. The cover of the cylinder is of hard rubber, *c*, containing binding screws for the attachment of the wires, and a small hole through which a thermometer can be passed to give the temperature of the interior space in which the muscle lies. In the end opposite to that in which the rubber cover fits is a narrow slot through which the silk thread attached to the tendon of the muscle passes to be fastened to the recording lever *g*, the thread passing over the pulley *e*. The muscle used in all the experiments was the gastrocnemius, and was dissected away from the *os cruris* in the usual way. It was placed horizontally upon an oblong block of wood, enclosed in a bit of the reflected skin, and was kept firmly in position by pinning the *os femoris* and *os cruris* to the wooden block. This method was used whether the muscle was entirely isolated from the rest of the body or whether the whole frog was placed in the warm chamber; and the muscle could easily be arranged so as to keep the circulation entirely uninjured. In one series of experiments the whole frog (curarized) was used, but so arranged that only the leg with the muscle to be experimented upon, with its circulation intact, was within the cylinder, the rest of the animal being placed upon a support just outside of the cylinder. This experiment required, of course, a different cover with a hole of sufficient size to allow the leg to fit snugly into it. The warm chamber was kept moist by means of filter paper saturated with normal NaCl solution, which was placed upon the block of wood beneath the muscle. The contractions of the muscle were registered upon the smoked paper of an ordinary drum kymograph, upon which also a time marker was made to write, recording fiftieths of a second. To prevent the great inertia fling of the muscle lever, a damper was attached, consisting of a fine steel rod attached to the lever and ending below in a disc of parchment paper, with a diameter of about 3.5 cms., which moved in a beaker of olive oil, *f*. For stimulating the muscle, one of the Du Bois Reymond induction coils was used, which was run with a single Daniells cell. For breaking the primary current through the coil, a mercury make-and-break key was employed, and the muscle in all the experiments was stimulated only by the breaking shocks, the making shocks being short-circuited in the usual way by means of a Du Bois Reymond key.

The stimulus was always a single sub-maximal shock, unless otherwise specified. A Centigrade thermometer was used for taking the temperature of the warm chamber.

Experiments.

In the following experiments the muscle was subjected to five different conditions. I have therefore tabulated the results as Series I, II, III, IV, V.

Series I.

In this series only the excised muscles of curarized frogs were used; muscles, therefore, in which there was no circulation of blood and the influence of motor nerves was eliminated. The muscle was prepared and placed in the cylinder and then slowly warmed. Starting from the temperature of the room, 21° to 23°, several contractions were taken at given intervals of temperature, and the muscle was kept at each temperature for about five minutes in order to be certain that the whole muscle had been really heated to that degree.

In this, as in the succeeding series of experiments, the following facts were ascertained whenever possible: 1. The temperature of the greatest contraction; 2. The temperature at which tetanic contractions appeared; 3. The temperature of the loss of irritability; 4. The duration of the loss of irritability; 5. The temperature of heat rigor, and, 6. The time required for the development of heat rigor at a constant temperature.

In general, the contractions show a gradual rise in height to a maximum in the highest simple contraction. At about this temperature contractions of a tetanic nature (see Plate IV, Fig. 3) were obtained in all but No. 2. Then there ensued a gradual diminution in the height of contractions until the irritability was lost. This condition may last for some time, as in No. 18 for 15 minutes, or it may give place at once to heat rigor. The latter develops slowly or quickly according as the temperature is kept at about the point at which the muscle loses its irritability, or is raised somewhat higher. In No. 1 the development of heat rigor required one hour, the temperature being constant at 38.5°. Where in the table the temperature of loss of irritability or of

heat rigor is given at a lower point than that of the highest contraction, the muscle had been previously heated to the highest point given. Plate IV, Fig. 2, gives a typical series of contraction curves, and although representing an experiment of Series II, may be taken as an illustration of the general effects of warmth upon frog's muscle under any one of the five conditions.

Series I.

Excised Muscle; Frog Curarized. 7 Experiments.

Number of Experiment.	Temperature of Highest Contraction.	Temperature of Tetanic Contractions.	Temperature of Loss of Irritability.	Duration of Loss of Irritability.	Temperature of Heat Rigor.	Time of Development of Rigor at a Constant Temperature.	Duration of Experiment.
1	36.25°	35.25°–38.25°	39°	....	38.50°	1 hour.	2 hrs. 15 minutes.
2	37.75°	....	37.75°	....	....	....	2 hrs. 35 "
3	36.25°	32.25°–37.75°	39.75°	....	39.75°	....	1 hr. 47 "
4	33.25°	26.25°–34.25°	34.25°	....	34.25°	....	1 hr. 45 "
18	38.25°	37.75°–38.25°	37.75°	15 minutes.	36.75°	....	3 hrs. 7 "
19	38.15°	37.75°–38.75°	38°	....	37.75°	....	1 hr. 26 "
20	37.75°	36.25°–38.50°	38.25°	....	....	....	1 hr. 20 "

In this series the highest contraction was obtained between 36.25° and 38.50°, except in one case, No. 4, which reached this point at 33.25°. No. 20 may be taken as an average experiment for this series, although from 21.75° to 33.50° there is generally a gradual rise in the height of contraction, while in this experiment the curves for this period present no material difference. The maximum contraction is given at 37.75°, while from 36.25° to 38.50° the muscle is in a state of great irritability, as shown by the tetanic nature of the contractions. At 39°, the temperature having reached its highest point, there is a complete loss of irritability. Without trying to keep the muscle in this condition for more than a few minutes, when it was taken from the case and cooled, the irritability was restored when the temperature fell to 33.75°. The contraction at this point is slightly higher than the contraction taken at about the same temperature near the beginning of the experiment. Subsequent warming resulted in diminishing contractions until the irritability was lost a second time at 38°.

Series II.

In this, as in Series I, only the excised muscles were used, but, as the frogs had not been curarized, the nerves were still active. Although the stimulus was sent directly to the muscle, probably the nerves received and distributed it. In this series there were no tetanic contractions.

SERIES II.

Muscle-Nerve. 4 Experiments.

Number of Experiment.	Temperature of Highest Contraction.	Temperature of Tetanic Contractions.	Temperature of Loss of Irritability.	Duration of Loss of Irritability.	Temperature of Heat Rigor.	Time of Development of Rigor at a Constant Temperature.	Duration of Experiment.
5	36.25°	....	36.50°	21 minutes.	36.50°	....	2 hrs.
6	29.25°	....	36.75°	....	36.75°	....	1 hr. 18 minutes.
16	37.75°	....	37.75°	....	39.25°	....	1 hr. 45 "
17	38.25°	....		....	....	....	2 hrs.

In No. 6 the second contraction at 29.75° was the highest, and the contractions then diminished as the muscle was warmed. To see if this diminution could be checked, at 36.25° the muscle was again cooled, but the irritability was only slightly restored. In No. 16, although the highest contraction was obtained at 37.75°, there was but a slight loss of irritability until at 39.25°, when heat rigor commenced.

During the first part of the development of rigor, contractions gradually decreasing in height were given. In No. 17 there is a typical series of contractions (see Plate IV, Fig. 2), gradually increasing in height until 38.25°. Then allowing the temperature to fall slightly, and keeping it constant at from 36.25° to 37° for about twenty minutes, the irritability did not remain constant, but steadily fell; even lowering the temperature still further was of no avail, and at 28.25° there was a total loss of irritability.

In all of these experiments there was some development of heat rigor, although very small, while the contractions were diminishing, so that this condition could not be marked off so distinctly as in the other series.

Series III.

In this series the muscle was dissected free from the distal attachment, but was left with the blood-vessels uncut at the proximal end. The whole frog having been curarized, was pinned to the block in such a manner that the circulation was not impaired, and then warmed. If the heart had ceased to beat when the muscle had lost its irritability, then, when the irritability of the muscle was restored by cooling and bathing in normal NaCl, the action of the heart was also generally restored. In these experiments the loss of irritability was somewhat more rapid than in those upon the excised muscles.

SERIES III.

Muscle with Circulation; Whole Frog Warmed; Frog Curarized. 7 Experiments.

Number of Experiment.	Temperature of Highest Contraction.	Temperature of Tetanic Contractions.	Temperature of Loss of Irritability.	Duration of Loss of Irritability.	Temperature of Heat Rigor.	Time of Development of Rigor at a Constant Temperature.	Duration of Experiment.
7	34.25°	....		....	33.75°	....	1 hr. 40 minutes.
8	34.25°	....		....	36.75°	....	1 hr. 6 "
9	35.75°	....	36.75°	1 hour.	....	....	3 hrs. 37 "
10	33.25°	....	37.25°	53 minutes.	39.25°	35 minutes.	4 hrs. 23 "
11	38.75°	37.75°–39.50°	39.25°	....	39.50°	1 hr. 28 min.	3 hrs. 14 "
12	36.75°	....	37.25°	7 minutes.	....	....	3 hrs. 5 "
21	37°	....	37°	36 minutes.	....	....	2 hrs. 38 "

In No. 7 the maximum contraction was at 34.75°. Raising the temperature, the irritability decreased, until at 35.75° only the faintest tremor could be obtained. Lowering the temperature to 29.25°, only the slightest irritability was shown, while at 26.75° there was none. Again raising the temperature, heat rigor commenced at 33.75°. Substantially the same results were obtained in No. 8, except that a loss of irritability came when the temperature had fallen to 29.25°, and heat rigor on again warming to 36.75°. In No. 9 the loss of irritability lasted for one hour, the temperature gradually falling. When the frog was taken from the warm chamber and bathed in normal salt solution, the irritability of the muscle was restored.

In No. 10 the loss of irritability was obtained twice—the first time at 37.25°, and then the muscle was allowed to cool off slowly. After 35 minutes, there being no irritability at 31.25°, the frog was taken from the case and cooled still more by bathing in normal NaCl. In 20 minutes at 23.75° the irritability was restored, and the muscle gave its highest contraction in this condition at that temperature. Again warming the frog, the irritability was a second time lost at 36.25°. Holding this temperature constant for 30 minutes, there was neither irritability nor heat rigor, but on increasing the temperature 2°, rigor commenced. Keeping the temperature constant at 39.25°, the development of heat rigor required 35 minutes.

In No. 11 marked tetanic contractions were obtained from 37.75° to 39.50°, but only after a rest of from two to five minutes between them, for stimuli sent in upon the next revolution of the drum after obtaining a tetanic contraction produced only the normal curve (see Plate IV, Fig. 3). In this experiment the development of heat rigor while the temperature remained at from 38.25° to 39.50° required 1 hour 28 minutes.

In No. 21 the highest contraction during the whole experiment was given at 32.25°, the muscle having been previously warmed to 36.25°, where the irritability was lost. The muscle was then kept constant in this condition at 36.25° to 37.25° for 36 minutes, and again the irritability was restored on cooling.

Series IV.

The frog pithed, and not curarized, was placed within the cylinder just as in Series III and gradually warmed. The circulation and the nerves of the muscle were therefore not directly impaired. As in the case of the experiments upon the muscle-nerve preparation, this series is marked by the absence of any tetanic contractions, which phenomenon therefore is no doubt due to the presence of the nerve.

SERIES IV.

Muscle with Circulation; Whole Frog Warmed; Frog Pithed. 3 Experiments.

Number of Experiment.	Temperature of Highest Contraction.	Temperature of Tetanic Contractions.	Temperature of Loss of Irritability.	Duration of Loss of Irritability.	Temperature of Heat Rigor.	Time of Development of Rigor at a Constant Temperature.	Duration of Experiment.
13	33.25°	....	37.75°	21 minutes.		....	2 hrs. 27 minutes.
14	32.75°	....	35.25°	....	....	....	2 hrs. 25 "
15	36.75°	....	37°	37 minutes.	....	....	2 hrs. 49 "

In No. 13, when the muscle had lost its irritability at 37.75°, although immediately cooled to 23.75°, only the faintest trace of irritability was restored, and that after 21 minutes; while heat rigor commenced slowly and continued as the muscle was again warmed. In No. 14, after the irritability was once lost, it was not restored. In No. 15 the muscle was kept at a temperature of 36° to 37.75° for 55 minutes before there was a loss of irritability, although heat rigor commenced after 27 minutes at 37.75°. Allowing the temperature to fall 0.75° in the next 28 minutes, heat rigor still continuing to a small extent, the loss of irritability was obtained. This condition was held for 37 minutes, during which time the muscle was cooling off, then the irritability was somewhat restored, but the muscle all the time developed more rigor. Again, as the temperature rose the rigor became more marked, but the muscle still retained its irritability until very near the end of the period.

Series V.

In this series the experiments without doubt were performed under the most favorable conditions. The frog was prepared as in Series III with perfect circulation, but, instead of warming the whole frog, only the leg including the muscle to be experimented upon was warmed.

The remainder of the body, resting upon a small shelf just outside of the cylinder, was kept cool by frequent bathing in normal NaCl solution. The fact that in No. 22 the muscle was

subjected to varying conditions of heat for five hours and twenty-five minutes without any rigor, shows that, although the muscle has lost its irritability and had been kept in this condition for a long time, yet if one is careful not to go beyond this point there is no apparent injury to the muscle from the influence of warmth.

SERIES V.

Muscle Only Warmed; With Circulation; Body Cool; Frog Curarized.
4 Experiments.

Number of Experiment.	Temperature of Highest Contraction.	Temperature of Tetanic Contractions.	Temperature of Loss of Irritability.	Duration of Loss of Irritability.	Temperature of Heat Rigor.	Time of Development of Rigor at a Constant Temperature.	Duration of Experiment.
22	34°	36.5°–36.75°	36.25°	30 minutes.			5 hrs. 25 minutes.
23	38.75°	36.7°–38.75°	39°				3 hrs. 13 "
24	39.25°	38.75°	38.75°				4 hrs. 47 "
25	....	....	....	....	41.75°	50 minutes.	1 hr. 17 "

In No. 22 the highest contraction was at 34°, but the following contraction at 35.75° was only one-quarter its height. Holding the temperature constant at from 35° to 37.12° for 1 hour 6 minutes, the contractions, taken about every five minutes, were almost exactly equal. Then raising the temperature not more than 1°, the irritability commenced to diminish until it was lost after 30 minutes at 36.25°. The temperature being kept at this high point, the state of loss of irritability remained without any heat rigor for 30 minutes. Then cooling the muscle, the irritability was partially restored immediately. Allowing the muscle to rest for 1 hour 10 minutes, the irritability was completely restored. Again warming it, tetanic contractions were given at 36.5° and 36.75° higher even than those given at 34° during the first part of the experiment. Again, holding the temperature constant at from 35° to 37.75° for 1 hour 45 minutes, the contractions were not quite uniform, there was a constant though slight diminution in the successive contractions until the period ended in complete loss of irritability.

In No. 23 the usual series was given; the highest contraction

at 38.75°, tetanic contractions from 36.37° to 38.75°, and loss of irritability at 39°. This was with a sub-maximal stimulus; but upon increasing the stimulus to maximal, a tetanic contraction higher than any preceding contraction was given. Keeping the temperature constant at from 38.75° to 41.25° for 1 hour 43 minutes, and using a maximal stimulus, the contractions gradually diminished, losing their tetanic nature after 25 minutes until the period ended in loss of irritability, while at the same time during this period the muscle had developed a large amount of its heat rigor. Now pushing the secondary coil completely over the primary, making the stimulus as much *supra-maximal* as possible, an additional small contraction was given, which was somewhat increased when the stimulus was sent in as rapidly interrupted induction shocks. In 26 minutes from the loss of irritability for a *maximal* stimulus even this enormous *supra-maximal* stimulus was unable to call forth a contraction.

Putting the frog, still cool and unharmed, aside in normal NaCl solution for about 14 hours, the irritability had again been partially restored, a maximal stimulus causing a contraction $\frac{1}{7}$ the height of the highest contraction, the stimulus being equal to that used in the first part of the experiment. Now warming the muscle to a high temperature, only a small curve of heat rigor was obtained. This would represent about one-third, and the curve of rigor obtained in the first portion of the experiment about two-thirds of all the rigor registered. But comparing this whole curve with the heat-rigor curve of the gastrocnemius from the other leg, which curve was considerably higher, shows that after taking the muscle from the cylinder some rigor must have developed which was not registered.

In No. 24, using a *maximal* stimulus from the beginning, a regular series of contractions reaching a maximum at 39.25° was obtained. From this point the temperature was held constant at from 39.25° to 38.75° for 1 hour 40 minutes. In 1 hour 8 minutes heat rigor commenced. At the end of this period the stimulus was made *supra-maximal*, but with scarcely any effect. However, when the muscle was cooled, bathed in normal NaCl and set aside for about 2 hours, the irritability was somewhat restored.

In one experiment upon a frog, not curarized nor pithed, the whole animal being warmed, a regular series of contractions

was obtained reaching a maximum at 36.75°. This highest contraction was also the only one in the whole experiment of a tetanic nature. In addition to these contractions caused by the regular single sub-maximal shocks there was an irregular series of voluntary contractions, increasing in height as the warmth increased until they too attained their maximum at 36.75°. But although the highest contractions, both voluntary and those caused by the electric stimulus, were obtained at the same temperature and about the same time, the former were 2½ times the height of the latter. In this condition of greatest irritability the frog gave a number of convulsive voluntary contractions which entirely ceased in about 5 minutes, while period B (see below) continued as in the other experiments.

Influence of Warmth upon the Irritability of Motor Nerves.

Three experiments were made upon motor nerves, using the same apparatus as in Series V, warming the sciatic nerve and registering its condition by means of the gastrocnemius, which rested upon the support outside, and was frequently bathed in normal NaCl solution.

In the first experiment with a single sub-maximal induction shock, the contractions showed no difference up to about 42.25° after having been warmed for 1 hour 23 minutes; then there was a slight diminution so that 33 minutes later at 48.75° a contraction was only given with rapidly interrupted induction shocks, and this irritability soon disappeared. Then, on allowing the nerve to cool, its irritability was restored. This process of warming to loss of irritability and then restoring was repeated several times with no apparent injury to the nerve.

The second experiment was practically a repetition of the first except that the diminution in height of the contractions commenced at 45.25°, and by holding the temperature constant within 1½° for 12 minutes a loss of irritability was obtained.

In the third, the nerve lost its irritability for a sub-maximal stimulus at 48.25°, and on continuing to warm it to 50° there was still no irritability manifested, until the stimulus was increased by pushing the secondary coil to "6"; then a contraction was

given. Still raising the temperature, the nerve again lost its irritability at 51.25° with the coil at "6," but at 51.75°, by pushing the secondary coil to "4," another contraction was obtained.

On now maintaining the temperature at this point for 4 minutes, irritability was lost for the stimulus "4." On again increasing the stimulus to "3½," a contraction of ⅓ the height of the last was given, but the response to this stimulus soon ceased.

Next, on warming to 53.25°, pushing the coil to "3" and making the stimulus tetanic, only a very small contraction resulted. This soon disappeared, and no further increase of stimulus was able to cause a contraction at this temperature, but as soon as the nerve was cooled the irritability returned, although somewhat impaired.

N. Afanasieff[8] in his paper, "Investigation upon the Influence of Warmth and Cold upon the Irritability of the Motor Nerves of the Frog," has emphasized several facts. His method was to let the nerve rest easily upon two hook-like stimulating electrodes placed within a glass tube. The warming was accomplished by bringing pure oil, heated to the desired temperature, in contact with the nerve. A minimal stimulus was used. The degree of irritability of the nerve was determined by moving the secondary coil. Gradually warming the nerve to 35° C. gave an increase of irritability. Suddenly warming the nerve to 35°–40° caused clonic spasms of the muscle. By warming to 40°–45° convulsions of a tetanic nature were produced, as Rosenthal also had observed. These convulsions may last for a minute. At 65° the irritability is destroyed almost immediately. Between 40° and 50° the irritability is lost, but can be restored upon cooling. This, Rosenthal and, according to Hermann,[9] Pickford also, had observed. A condition which Afanasieff calls the "apparent death of the nerve," wherein it is absolutely unexcitable to the *strongest* stimuli, is obtained at 50°–65° C. But by cooling the nerve the irritability can be restored, though incompletely.

There are several differences between the results of Afanasieff's work and those of this paper, the methods being quite unlike in the two cases. The highest temperature at which I could get a contraction with the strongest stimulus was at 53.25° C., and beyond that the nerve went into "the condition of apparent death."

When the irritability was lost with a sub-maximal stimulus, not only was a contraction given at the same temperature by increasing the stimulus, but also at a somewhat higher temperature. And this process of losing and regaining the irritability was repeated at successively higher temperatures until the limit was reached.

Conclusions.

In general, four periods, representing distinct phases of the condition of irritability, were obtained in each of the five series. These may be described as, *A*, gradual increase of irritability to the maximum; *B*, gradual diminution of irritability to its total loss; *C*, condition of no irritability, and *D*, development of heat rigor. In these separate phases the results of the whole course of experiments may be summarized.

Period A.

Gradual Increase of Irritability to the Maximum.

This in general corresponds to Marey's[2] first period "excitation of muscular action," in which he obtained the highest contractions at from 30° to 35°. But my results differ in making the maximum contractions at from 32.75° to 39.25°, with only one exception, No. 6, Series II, where it was 29.25°, and this no doubt was abnormal. Marey also says that if a muscle be previously submitted to a low temperature and then warmed, the descent of the contraction curve becomes shortened, thus marking the transition between the lengthening of movement by cold and its acceleration by warmth. This is evidently true for this epoch of transition; but from the temperature at which the muscle enters into period A, say 22°–26°, there is generally a slight *increase* in the duration of the contraction, so that the contraction lasts .02 or .03 of a second longer in the condition of greatest irritability than it does at the beginning of period A. In addition to Marey's results, during and near the temperature of greatest irritability, I obtained tetanic contractions, the stimulus being simply a single *sub-maximal* shock. These tetanic contractions were obtained in ten experiments included in Series I, III and V, but not in either Series II or IV, so that

whenever the *uninjured* nerve was present they were absent. As shown in the experiments on nerves, at a period when the muscle is in its condition of greatest irritability the nerve is scarcely affected by heat. Hence, as the nerve probably received and distributed most of the stimulus, this may explain the apparent anomaly. These tetanic contractions were usually more marked after a rest of four or five minutes than in contractions observed after a shorter rest, as one or two minutes, and they sometimes disappeared entirely in the latter case.

Period B.

Gradual Diminution of Irritability to Total Loss.

In Marey's second period, "alteration of the muscle by warmth, and loss of irritability," the phases in periods B and C were united, while period D was not brought out at all.

In period B there is a gradual diminution in both the height and duration of the contraction. If one is very careful to stop the rise of temperature immediately after the highest contraction and at that point keep it constant, this period may last for one or two hours. If, however, the temperature rises only one or two degrees above that at the beginning of the period, the loss of irritability is considerably hastened, and heat rigor may commence. Exercising considerable care, however, this period may be carried into period C without causing any rigor in the muscle.

Period C.

Condition of No Irritability.

This period was pointed out by the investigation of Schmulewitsch,[(3)] whose methods have been described. Schmulewitsch, however, did not keep the muscle in this condition as I have done, but restored its irritability at once by means of cool 0.65 per cent. NaCl solution. Normal NaCl is not necessary to restore the irritability, although it promotes the restoration. Simple cooling is sufficient.

This period may come at any point within 5° above the temperature of the greatest contraction (in No. 6, Series II, there was a difference of 7°), or it may come at a somewhat lower

degree if, after period B is well begun, the temperature is allowed to fall. I have found that this period may last if the temperature is kept constant, as *e. g.* No. 21, Series III, for 36 minutes or more; while, if the temperature be allowed to fall slowly, as *e. g.* No. 9, Series III, it may last for one hour.

Period D.

Development of Heat Rigor.

After the restoration of the muscle's irritability, the extent of the contractions is generally smaller than that of those of period A, the first contraction being usually the largest; then they diminish until a second loss of irritability. To this, however, there are marked exceptions, in one or the other particular, or in both, as *e. g.* No. 22, Series V, where the conditions of the experiment were more favorable than in the preceding series. This *restored* series may be obtained without any heat rigor, but a loss of irritability usually comes sooner than in period B. Heat rigor commences generally at a temperature from 5° to 1° or 2° above that of loss of irritability; but if in period C the muscle be kept sufficiently long at a constant temperature, no further increase is necessary to produce heat rigor. The time of development of rigor at a constant temperature varies from 35 minutes, as *e. g.* No. 10, Series III, to 1 hour 28 minutes, as *e. g.* No. 11, Series III.

The regular series of long contractures which Marey[2] obtained during the development of heat rigor I was unable to get. Unfortunately, Marey does not give us the exact method by which his curves were obtained. During the first portion of the development of rigor, contractions can be obtained, but they do not show long contractures. However, if a period of rest intervenes, a contraction then taken may give the long contracture; but the curve of the succeeding contraction, taken after one revolution of the registering drum, generally, as in the normal curve, comes at once back to the base line. The long-lasting contracture is exceptional.

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EXPLANATION OF PLATE IV.

FIGURE 1. Apparatus used in warming the frog's muscle (described page 20).

FIGURE 2. Showing the effect of gradual increase of temperature upon the contractions of the muscle. The temperatures indicated by the different letters are as follows:

a,	26.25°	*e*,	37.25°	*i*,	37°	*m*,	31.75°
b,	30.75°	*f*,	36.75°	*j*,	36.25°	*n*,	30.25°
c,	34.75°	*g*,	38.25°	*k*,	36.75°	*o*,	29.25°
d,	36.75°	*h*,	36.25°	*l*,	33.75°	*p*,	28.25°

FIGURE 3. Showing the tetanic contractions obtained with single induction shocks. The temperatures indicated by the letters are as follows: *f*, 37.25° *g*, 37.75°.

Fig. 1

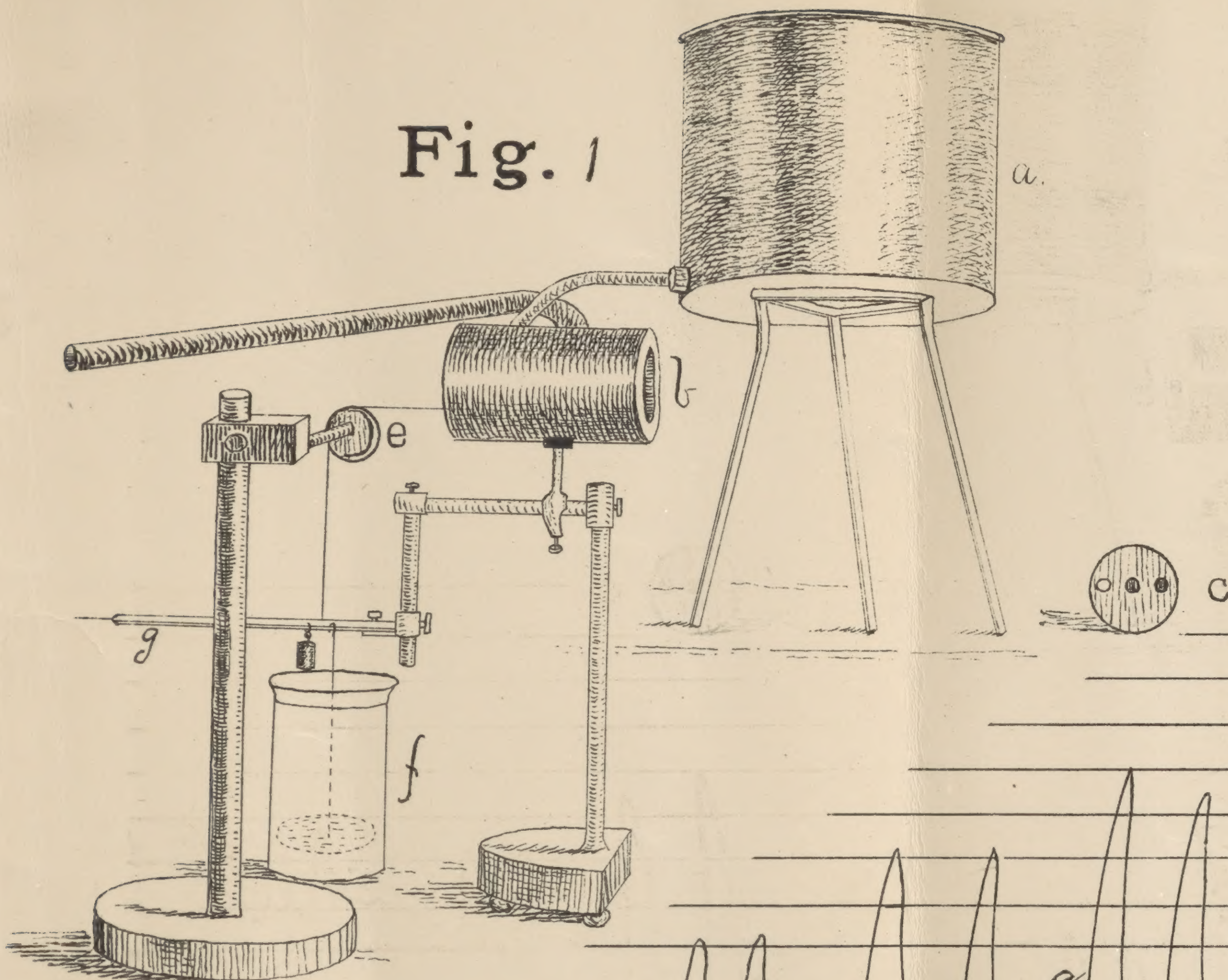

Fig 2.

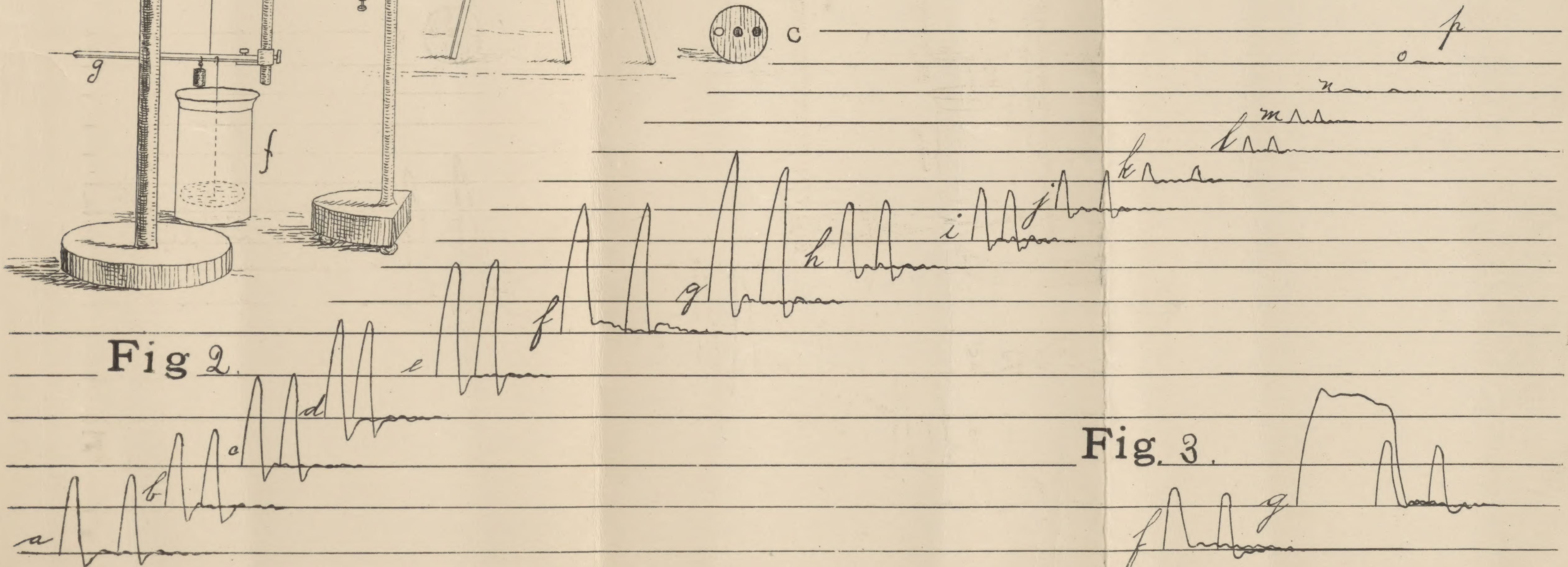

Fig. 3.